

Part I. The Interaction of the Acid Chloride of
2-Benzoylbenzoic Acid with Phenols: (a) Aryl
Esters and Phenylaryloxyphthalides;
(b) Diarylphthalides. Part II.
Derivatives of 9-Hydroxy-9-
phenylanthrone-10

A DISSERTATION

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The Interaction of the Acid Chloride of 2-Benzoylbenzoic Acid with Phenols. I. Aryl Esters and Phenylaryloxyphthalides¹

By F. F. BLICKE AND R. D. SWISHER²

It has been shown that the phenyl ester of 2-(4'-methoxybenzoyl)-benzoic acid rearranges readily and practically quantitatively, under the influence of aluminum chloride, to yield phenolphthalein.³ It now seemed desirable to determine whether or not aryl esters of 2-benzoylbenzoic acid, in general, could be transformed by aluminum chloride into diarylphthalides.

We began our investigation with a study of the phenyl ester of 2-benzoylbenzoic acid. The preparation of the latter substance was attempted by three methods: interaction of the acid chloride with (a) potassium phenolate, (b) with phenol and (c) with phenol in the presence of pyridine. Instead of the mere formation of the phenyl ester three isomeric products were obtained, the nature and quantity of each dependent, in general, upon the method employed. One of the products was 4'-hydroxydiphenylphthalide; the other two were, presumably, the true phenyl ester and phenylphenoxyphthalide, respectively.⁴

It was impossible to differentiate the phenyl ester from the phenylphenoxyphthalide by chemical means; both compounds are hydrolyzed by alkali with the formation of 2-benzoylbenzoic acid and phenol. The hydrolysis of the phenoxyphthalide may be explained by the following formulation.

When heated with aluminum chloride, or mixed with concd. sulfuric acid, the ester and the phenoxyphthalide both yielded 4'-hydroxydiphenylphthalide.

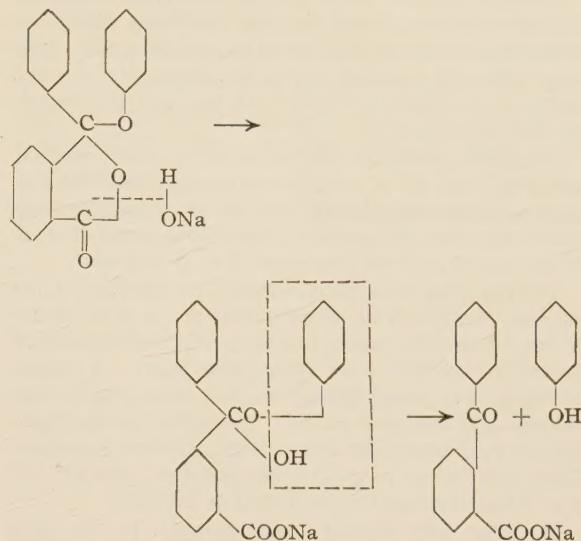
(1) This paper represents the first part of a dissertation to be submitted to the Graduate School by Mr. Swisher in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the University of Michigan.

(2) The Upjohn Company Fellow.

(3) Blicke and Weinkauff, *THIS JOURNAL*, **54**, 331 (1932).

(4) An intensive study has been made by others of alkyl esters of various 2-benzoylbenzoic acids and the existence of two isomeric forms—a ketoid (true ester) and a lactoid (phenylalkoxyphthalide)—established [Meyer, *Monatsh.*, **25**, 475, 1177 (1904); Hantzsch and Schwiete, *Ber.*, **49**, 215 (1916); Hantzsch, *ibid.*, **52**, 1572 (1919); and others]. In these instances the particular modification of the ester obtained depended upon the manner in which the acid chloride had been prepared, and only one modification was formed in any given reaction.

Our results in the case of phenol and 2-benzoylbenzoic acid are decisively different in that the same reaction products (both forms of the ester) were produced regardless whether the acid chloride had been prepared by the use of thionyl chloride, phosphorus pentachloride or by chlorination of phenylphthalide.



Reaction of the acid chloride of 2-benzoylbenzoic acid with six other phenols was studied; in all instances, except one, an ester and a phenylaryloxyphthalide were obtained and in some cases a diarylphthalide⁵ was also produced.

Experimental Part

The general procedure (a) is illustrated below in the case of phenol and the acid chloride of 2-benzoylbenzoic acid.

The products obtained with various phenols are recorded in Table I.

(a) **The Acid Chloride and the Potassium Derivative of the Phenol.**—A mixture of 27 g. of 2-benzoylbenzoic acid and 29 g. of thionyl chloride (Pract.) was allowed to react for twelve hours, unchanged thionyl chloride removed under diminished pressure,⁶ the chloride dissolved in dry, thiophene-free benzene; potassium phenolate,⁷ prepared from 17 g. of phenol, 6.9 g. of potassium and 400 cc. of absolute ether was added.⁸ After twelve hours the material was filtered through a Jena filter, the filtrate

(5) The diarylphthalides will be discussed in Part II of this paper.

(6) The first eight times the chloride was prepared it was obtained as an oil, but in all subsequent experiments the material crystallized spontaneously. The chloride was washed several times with small amounts of absolute ether.

(7) In order to obtain the phenolate free from unchanged phenol it was prepared in a specially constructed side-arm flask fitted with a stirrer and a reflux condenser. The phenolate was filtered through a Jena filter and washed thoroughly with absolute ether. Special precautions were observed to prevent contact with atmospheric moisture.

(8) In the case of all other phenols 500 cc. of benzene was used instead of ether and the mixture was heated.

shaken with sodium hydroxide solution, the benzene-ether layer separated and the solvents removed. The residue, 30 g., was boiled with ether and the insoluble portion recrystallized from alcohol; m. p. 162–163°; yield 4 g. The solvent was removed from the ether extract and the residue, 24.5 g., recrystallized from alcohol; m. p. 80–82°.

Since some of the esters and arylaryloxyphthalides are insoluble in ether and benzene, the precipitate which contained the potassium chloride was placed in a dish; after some time the material was added, cautiously in small portions, to sodium hydroxide solution and the organic product recrystallized.

Potassium phenolate was added to the acid chloride, prepared from 27 g. of 2-benzoylbenzoic acid, 24.5 g. of phosphorus pentachloride and 300 cc. of carbon disulfide;⁹ there was obtained 24 g. of the compound of m. p. 80–82° and 4 g. of the compound of m. p. 162–163°.

The following experiment describes the behavior of the chloride obtained from phenylphthalide. A slow stream of dry chlorine was passed into 25 g. of phenylphthalide,¹⁰ heated to 115–120°,¹¹ for twenty-four hours. A stream of dry air was passed through the hot mixture to remove chlorine and hydrogen chloride, the yellow, sirupy liquid dissolved in benzene and treated with potassium phenolate. There was formed 18 g. of the product of m. p. 80–82° and 3 g. of the compound which melted at 162–163°.

(b) **The Acid Chloride and Phenol.**—To the acid chloride, obtained from 0.1 mole of 2-benzoylbenzoic acid, there was added 0.1 mole of the phenol, dissolved or suspended in 150 cc. of benzene. After eighteen hours any crystalline material present was triturated with 10% sodium hydroxide solution, washed with water and recrystallized. The benzene filtrate was shaken with alkali, then with water, dried and the solvent removed. The oily residue became crystalline when cooled and treated with a small amount of ether.

In the case of phenol, α - and β -naphthol this method yielded only a diarylphthalide.

(c) **The Acid Chloride, the Phenol and Pyridine.**—The acid chloride, obtained from 0.1 mole of the acid, was dissolved in benzene and added to 0.1 mole of phenol, dissolved in 25 cc. of dry pyridine. After two to six days the reaction mixture contained a precipitate of pyridine hydrochloride, in some cases admixed with ester. The mixture was treated with 30 cc. of concd. hydrochloric acid, shaken thoroughly and any insoluble material removed and treated separately. The benzene layer was shaken twice with 30-cc. portions of hydrochloric acid and then with sodium carbonate solution; insoluble material was removed and purified. Finally, the benzene layer was shaken with sodium hydroxide solution, in order to extract any hydroxydiarylphthalide present, washed with water, dried, the solvent removed and the product purified.

Interaction of the Phenyl Ester and Phenoxyphthalide with Aluminum Chloride and with Sulfuric Acid.—Since the ester and the phthalide reacted in the same manner, these processes are illustrated only in the case of the lower

melting product. A mixture of 2 g. of the compound, 2 g. of anhydrous aluminum chloride and 10 cc. of tetrachloroethane was heated at 100° for five hours, the mixture treated with ice and steam distilled. The residue was dissolved in 10% sodium hydroxide solution, filtered

TABLE I
ARYL ESTERS AND PHENYLARYLOXYPHTHALIDES

Phenol used	M. p., °C., of ester or phthalide ^a	Method used ^{b,c}	Color with concd. H ₂ SO ₄ ^d
Phenol	(1) 80–82	(a) (c)	Orange
Phenol	(2) 162–163	(a) (c)	Orange
4-Bromophenol	(3) 92–94	(c)	Yellow-green, green, orange
4-Bromophenol	(4) 170–172	(b)	Green, dark green, yellow
Thiophenol	(5) 112–113	(a)	Deep red
Thiophenol	(6) 117–118	(b)	Deep red
<i>o</i> -Xenol	(7) 103–105	(a) (c)	Orange-red
<i>o</i> -Xenol	(8) 195–197	(b) (c)	Orange-red
<i>p</i> -Xenol	(9) 163–165	(a) (c)	Orange-pink, violet, red-brown
<i>p</i> -Xenol ^e	(10) 117–119	(a) (b) (c)	Purple, violet, red- violet
α -Naphthol	(11) 102–104	(a) (c)	Orange, violet, green- brown
β -Naphthol	(12) 103–105	(a) (c)	Yellow-green, red- green, green-brown
β -Naphthol	(13) 198–199	(c)	Green, green-brown

Com- pound	Formula	Analyses, %	
		Calcd.	Found
1	C ₂₀ H ₁₄ O ₃	C, 79.45; H, 4.67	C, 79.34; H, 4.68
2	C ₂₀ H ₁₄ O ₃	C, 79.45; H, 4.67	C, 79.24; H, 4.82
3	C ₂₀ H ₁₃ O ₃ Br	Br, 20.98	Br, 21.07
4	C ₂₀ H ₁₃ O ₃ Br	Br, 20.98	Br, 20.90
5	C ₂₀ H ₁₄ O ₂ S	S, 10.08	S, 10.09
6	C ₂₀ H ₁₄ O ₂ S	S, 10.08	S, 10.16
7	C ₂₈ H ₁₈ O ₃	C, 82.51; H, 4.80	C, 82.58; H, 4.81
8	C ₂₈ H ₁₈ O ₃	C, 82.51; H, 4.80	C, 82.62; H, 4.72
9	C ₂₈ H ₁₈ O ₃	C, 82.51; H, 4.80	C, 82.55; H, 4.76
10	C ₂₈ H ₁₈ O ₃	C, 82.51; H, 4.80	C, 82.45; H, 4.78
11	C ₂₄ H ₁₆ O ₃	C, 81.79; H, 4.58	C, 81.70; H, 4.58
12	C ₂₄ H ₁₆ O ₃	C, 81.79; H, 4.58	C, 81.92; H, 4.54
13	C ₂₄ H ₁₆ O ₃	C, 81.79; H, 4.58	C, 81.61; H, 4.41

1. Calcd. mol. wt., 302; found, 303 (benzene, Menzies' method).

2. Calcd. mol. wt., 302; found, 309 (benzene, Menzies' method).

When hydrolyzed with alcoholic sodium hydroxide 0.0854 g. of compound 1 yielded 0.0266 g. of phenol (U. S. P. X method); calcd. 0.0266 g. From 0.1037 g. of compound 2 there was obtained 0.0321 g. of phenol; calcd. 0.0322 g. In each instance the 2-benzoylbenzoic acid formed was identified by its melting point.

All of the other compounds listed above yielded, upon hydrolysis, the corresponding phenol and 2-benzoylbenzoic acid.

^a Compounds 1, 3, 5, 6, 7 and 10 were recrystallized from alcohol; compounds 11 and 12 from alcohol which contained a small amount of acetic acid; compounds 2, 4, 8 and 9 from acetic acid; compound 13 from ethyl acetate.

^b The highest yield was obtained in the method italicized.

^c The isomeric compounds obtained by the use of *o*-xenol, *p*-xenol and β -naphthol, respectively, in method (c) can be separated by the use of alcohol since the higher melting compound is much less soluble.

^d The first color was obtained with cold acid, the second when the mixture was warmed, the third when the mixture cooled.

^e By use of method (c) an alkali-insoluble gum was also obtained which, upon hydrolysis, yielded α -naphthol and 2-benzoylbenzoic acid.

(9) Haller and Guyot, *Bull. soc. chim.*, [3] 25, 54 (1901).

(10) Ullmann, *Ann.*, 291, 23 (1896).

(11) At higher temperatures we found that anthraquinone was formed.

and the filtrate acidified. The precipitate was dissolved in acetic acid and the solvent allowed to evaporate. The material, 4'-hydroxydiphenylphthalide, was recrystallized from acetic acid; mixed m. p. 165-167°.¹²

A solution was made of 5 g. of the lower melting compound in 25 cc. of concd. sulfuric acid; after one-half hour the solution was poured onto ice, the cold mixture filtered, the granular product dissolved in benzene, the solution shaken with sodium carbonate solution and then extracted with 10% sodium hydroxide. Upon acidification of the latter 4 g. of 4'-hydroxydiphenylphthalide was obtained of m. p. 165-166°.

(12) Baeyer [*Ann.*, **354**, 173 (1907)] recorded the melting point as 167°.

Summary

The interaction of the acid chloride of 2-benzoylbenzoic acid with (a) the potassium derivative of various phenols, with (b) the phenols alone and with (c) the phenols in the presence of pyridine was studied. In general it may be stated that three isomeric compounds are produced—two compounds which are presumably the aryl ester of benzoylbenzoic acid and the phenylaryloxyphthalide, respectively, and the hydroxydiarylphthalide.

ANN ARBOR, MICH.

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The Interaction of the Acid Chloride of 2-Benzoylbenzoic Acid with Phenols. II. Diarylphthalides¹

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It has been found³ that the acid chloride of 2-benzoylbenzoic acid reacts at ordinary temperature with potassium phenolate or with phenol in the presence of pyridine to yield compounds which are presumably the phenyl ester of the benzoylbenzoic acid and the isomeric phenylphenoxyphthalide; analogous results were obtained with other phenols.

In this investigation it has been shown that when the acid chloride and phenol alone or anisole is used 4'-hydroxy- and 4'-methoxydiphenylphthalide, respectively, are obtained. Certain other phenols and their methyl ethers act similarly; however, in the case of *o*-xenol, *p*-xenol and 4-bromophenol the addition of aluminum chloride is necessary, otherwise an ester or arylaryloxyphthalide is formed. It was not found possible to obtain from thiophenol a diarylphthalide which contained the mercapto group.⁴

In several instances the acid chlorides of 2-(4'-hydroxybenzoyl)- and of 2-(4'-methoxybenzoyl)-benzoic acid were used.

The diarylphthalides obtained are listed in Table I.

It seemed desirable to synthesize 2-(4"-hydroxybenzoyl)-benzophenone in order to compare its properties with those of the isomeric 4'-hydroxydiphenylphthalide, especially since the preparative procedures used for the latter substance, in themselves, do not offer rigid proof of the phthalide structure—2-benzoylbenzoic acid and its acid chloride react in the keto as well as in the lactoid form. Inasmuch as it was necessary to prepare 2-(4"-hydroxybenzoyl)-benzophenone in the form of its methyl ether and since the demethylation product of the latter could not be obtained in crystalline form, the properties of 2-(4"-methoxybenzoyl)-benzophenone were compared with those of 4'-methoxydiphenylphthalide. The melting point of the methoxy phthalide is

110–115°, that of the methoxy ketone 132–135°; the phthalide yields an orange solution with concd. sulfuric acid, the ketone a deep violet solution.

Various investigators have found it exceedingly difficult, by the use of procedures described hitherto, to obtain 4'-hydroxy-, 4'-methoxy- and 4-hydroxy-4"-methoxydiphenylphthalide in crystalline form. By means of the synthesis described in this paper these phthalides are obtained as crystalline products directly from the reaction mixtures in practically quantitative yields.

Experimental Part

Diarylphthalides.—To the acid chloride obtained from 0.1 mole of the benzoylbenzoic acid and thionyl chloride⁵ there was added 0.1 mole of the phenol or the aryl methyl ether, dissolved or suspended in 150 cc. of benzene. After thirty-six hours⁶ the mixture was filtered,⁷ the filtrate shaken with 10% sodium carbonate solution and then with 10% sodium hydroxide solution to extract the hydroxydiarylphthalide, which is subsequently obtained by acidification. If a methoxydiarylphthalide is formed it remains in the benzene layer; after removal of the solvent and treatment of the cooled residue with a small amount of ether, it practically always crystallized.

2-(4"-Methoxybenzoyl)-benzophenone.—A mixture of 100 g. of 2-benzoylbenzoic acid⁸ and 100 g. of lead thiocyanate⁹ was heated in a 250-cc. distillation flask in a bath at 200° for one hour and the mixture then distilled. The distillate (300–325°),¹⁰ combined with the large amount of material obtained by extraction of the residue in the distillation flask with benzene, was fractionated. The 2-cyanodiphenylmethane obtained boiled at 315–320°,¹¹ yield 40 g.

A crystalline precipitate formed when 15 g. of the

(5) The acid chloride of 2-benzoyl- and of 2-(4'-methoxybenzoyl)-benzoic acid was obtained in crystalline condition.

(6) In the case of phenol and α -naphthol the reaction was complete at the end of one-half hour.

(7) In some instances the phthalides separate spontaneously from the reaction mixture in crystalline form.

(8) Barnett, Cook and Nixon, *J. Chem. Soc.*, 508 (1927).

(9) Reed, *Am. Chem. J.*, **43**, 180 (1910).

(10) A small amount of crystalline material present was removed by filtration and recrystallized from benzene; m. p. 162–163°. This product, was undoubtedly, the acid amide of 2-benzoylbenzoic acid; Cassirer [*Ber.*, **25**, 3022 (1892)] stated that this compound melts at 163°.

(11) Cassirer [*Ber.*, **25**, 3021 (1892)] obtained the cyanide by another method and reported the boiling point to be 313–314°. In order to identify the cyanide prepared by us it was allowed to react with phenylmagnesium bromide whereupon 2-benzoyldiphenylmethane was formed [Seidel, *ibid.*, **61**, 2275 (1928)].

(1) This paper represents the second part of a dissertation to be submitted to the Graduate School by Mr. Swisher in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the University of Michigan.

(2) The Upjohn Company Fellow.

(3) Part I. Blicke and Swisher, *THIS JOURNAL*, **56**, 902 (1934).

(4) Knapp [*Monatsh.*, **58**, 176 (1931)] tried unsuccessfully to prepare thiophenolphthalidein (4',4"-dimercaptodiphenylphthalide).

TABLE I
DIARYLPHTHALIDES

A = Acid chloride of 2-benzoylbenzoic acid
 B = Acid chloride of 2-(4'-hydroxybenzoyl)-benzoic acid
 C = Acid chloride of 2-(4'-methoxybenzoyl)-benzoic acid

Chloride	Phenol or ether	Phthalide	M. p., °C.	Color with ^a concd. H ₂ SO ₄
A	Phenol	(1) 4'-Hydroxydiphenyl	168-170	Orange
A	Anisole	(2) 4'-Methoxydiphenyl	110-115	Orange
A	4-Bromophenol ^b	(3) 2'-Hydroxy-4'-bromodiphenyl	210-211	Green, yellow-green
A	2,6-Dibromophenol ^b	(4) 4'-Hydroxy-3',5'-dibromodiphenyl	199-200	Orange-red
A	<i>o</i> -Xenol ^b	(5) Phenyl- <i>o</i> -hydroxyphenyl	178-180	Orange-red
A	<i>o</i> -Xenyl methyl ether	(6) Phenyl- <i>o</i> -methoxyphenyl	152-154	Orange-red
A	<i>p</i> -Xenol ^b	(7) Phenyl- <i>p</i> -hydroxyphenyl	220-222	Green, brown
A	<i>p</i> -Xenyl methyl ether	(8) Phenyl- <i>p</i> -methoxyphenyl	179-180	Green, brown
A	α -Naphthol	(9) Phenyl- α -hydroxynaphthyl	231-233	Purple, brown
A	α -Naphthyl methyl ether	(10) Phenyl- α -methoxynaphthyl	206-207	Purple, brown
A	β -Naphthol	(11) Phenyl- β -hydroxynaphthyl	234-236	Indigo, brown
A	β -Naphthyl methyl ether	(12) Phenyl- β -methoxynaphthyl	210-212	Indigo, brown
B	Phenol	(13) 4',4''-Dihydroxydiphenyl	253-256	Red
B	Anisole	(14) 4'-Hydroxy-4''-methoxydiphenyl	139-142	Red
C	Phenol	(14) 4'-Hydroxy-4''-methoxydiphenyl	139-142	Red
C	Anisole	(15) 4',4''-Dimethoxydiphenyl	97-99	Red

ANALYSES^c

Compound	Formula	Calcd., %			Found, %		
		C	H	OCH ₃	C	H	OCH ₃ ^d
2	C ₂₁ H ₁₆ O ₃	79.71	5.10	9.81	79.58	4.92	9.92
3	C ₂₀ H ₁₃ O ₃ Br	(Br, 20.97)			(Br, 20.98)		
5	C ₂₆ H ₁₈ O ₃	82.51	4.80		82.31	4.76	
6	C ₂₇ H ₂₀ O ₃	82.62	5.14	7.91	82.47	5.03	8.28
7	C ₂₆ H ₁₈ O ₃	82.51	4.80		82.26	4.77	
8	C ₂₇ H ₂₀ O ₃	82.62	5.14	7.91	82.23	4.99	7.93
9	C ₂₄ H ₁₆ O ₃	81.79	4.58		81.62	4.49	
10	C ₂₅ H ₁₈ O ₃	81.93	4.96	8.47	81.70	4.87	8.52
11	C ₂₄ H ₁₆ O ₃	81.79	4.58		81.75	4.61	
12	C ₂₅ H ₁₈ O ₃	81.93	4.96	8.47	81.56	4.87	8.52

Compound 6, mol. wt. calcd. 392; found 395 (benzene, Menzies method).

^a The first color is obtained with cold acid, the second color with hot acid.

^b In the case of this compound the reaction was carried out in the presence of one mol. equiv. of aluminum chloride in tetrachloroethane; in the absence of the condensation agent the ester or arylaryloxyphthalide is formed.

^c Prior to analysis all samples were dried at 125° under diminished pressure in a current of dry nitrogen.

^d In the methoxy determinations phenol was used as a solvent [Weishut, *Monatsh.*, **33**, 1165 (1912)].

COMMENTS

Compounds 1-13 inclusive were recrystallized from acetic acid, compound 15 from alcohol.

Compound 2. Meyer and Fischer [*Ber.*, **44**, 1953 (1911)] recorded the melting point as 86°. The compound appears to contain benzene of crystallization which is lost gradually at room temperature. When dried at an elevated temperature the material changes into a somewhat sticky mass. The identity of our compound was established by boiling 5 g. of the material for six hours with 40 cc. of acetic acid and 25 cc. of 48% hydrobromic acid; the 4'-hydroxydiphenylphthalide obtained melted at 168-170°, while Baeyer [*Ann.*, **354**, 173 (1907)] stated that this compound melts at 167°.

Furthermore, reduction of compound 2 to 4'-methoxytriphenylmethane-2-carboxylic acid was effected as follows: 10 g. of 4'-methoxydiphenylphthalide, dissolved in alcohol, was added to 200 cc. of 10% sodium hydroxide solution, the mixture diluted to 500 cc., 50 g. of zinc dust added

and the mixture heated for twelve hours on a steam-bath. The mixture was filtered, the acid precipitated from the filtrate, filtered, dissolved in 10% sodium carbonate solution, filtered and the acid again precipitated with hydrochloric acid. The crude, pasty product was dried at 100° for twelve hours and recrystallized from dilute alcohol; m. p. 146-147°.

Anal. Calcd. for C₂₁H₁₈O₃: C, 79.21; H, 5.70; equiv. wt., 318. Found: C, 79.22; H, 5.68; equiv. wt., 325.

When 1 g. of the acid was boiled for three hours with 8 cc. of acetic acid and 5 cc. of 40% hydrobromic acid the 4'-hydroxytriphenylmethane-2-carboxylic acid obtained melted at 209-210°¹² after recrystallization from dilute alcohol.

Compound 3. Upon reduction of this substance with zinc dust in alkaline solution, as described above, a bromine-free, bicarbonate-soluble product, undoubtedly

(12) V. Pechmann [*Ber.*, **13**, 1616 (1880)] recorded the melting point as 210°.

2'-hydroxytriphenylmethane-2-carboxylic acid, was obtained; m. p. 194–196° after recrystallization from dilute alcohol.

Anal. Calcd. for $C_{20}H_{16}O_3$: C, 78.91; H, 5.30; equiv. wt., 304. Found: C, 79.18; H, 5.45; equiv. wt., 306.

To obtain the corresponding methyl ether, 2'-methoxytriphenylmethane-2-carboxylic acid, 5 g. of the material, dissolved in 15 cc. of 10% sodium hydroxide solution, was heated with 4 cc. of dimethyl sulfate for a short time; 2 g. of sodium hydroxide and 10 cc. of water were added and the mixture heated for three hours. The solution was acidified, the precipitate dissolved in 10% sodium carbonate solution, the acid precipitated with hydrochloric acid and recrystallized from alcohol; m. p. 191–193°.

Anal. Calcd. for $C_{21}H_{18}O_3$: C, 79.21; H, 5.70. Found: C, 78.96; H, 5.73.

Compound 4. This substance has been prepared by bromination of 4'-hydroxydiphenylphthalide by v. Pechmann [*Ber.*, **13**, 1615 (1880), m. p. 196°] and by Acree and Slagle [*Am. Chem. J.*, **42**, 138 (1909), m. p. 199°]. Our preparative method definitely establishes the positions occupied by the bromine atoms.

Compounds 5, 7, 9 and 11 upon methylation yielded the corresponding methyl ethers; from compounds 2, 6, 8 and 14 the corresponding hydroxy phthalides were obtained after demethylation.

Compounds 5 and 7 dissolve in alkali to form a yellow solution while compounds 9 and 11 yield an orange solution.

Compound 14. The melting point recorded in the table was obtained with material taken directly from the reaction mixture. Meyer and Spengler [*Ber.*, **38**, 1328 (1905)] stated that the compound melted at 141–142°; Green and King [*ibid.*, **40**, 3729 (1907)] recorded the melting point as 148–149°; see also Lund, *J. Chem. Soc.*, 1572 (1928).

Compound 15. Grande [*Gazz. chim. ital.*, **26**, I, 224 (1896)] reported the melting point as 101–102°.

cyanide was heated with the Grignard reagent prepared from 38 g. of *p*-iodoanisole, 3.9 g. of magnesium, 60 cc. of benzene and 60 cc. of ether. The precipitate and the benzene-ether layer were decomposed separately in the usual manner and the gummy 2-(4"-methoxybenzoyl)-diphenylmethane obtained was steam distilled to remove anisole; m. p. 68–70° after recrystallization from alcohol.

To obtain 2-(4"-methoxybenzoyl)-benzophenone a mixture of 32 g. of the methane, 300 cc. of concd. nitric acid and 600 cc. of water was boiled for three hours, poured into water and the gummy product stirred with ether, whereupon it partially crystallized. It was filtered, washed with ether and recrystallized from acetic acid; m. p. 133–135°; yield 13 g. The solvent was removed from the ether solutions and the residue reoxidized; 12 g. more of the product was obtained.

Anal. Calcd. for $C_{21}H_{16}O_3$: C, 79.71; H, 5.10; mol. wt., 316. Found: C, 79.36; H, 5.11; mol. wt., 318 (benzene, Menzies method).

A diazine, 3-phenyl-6-(*p*-methoxyphenyl)-4,5-benzopyridazine, was formed when 3 g. of the ketone was boiled with 8 g. of 40% hydrazine and 30 cc. of acetic acid for five hours, the mixture poured into water and the precipitate recrystallized from acetone; m. p. 157–159°.

Anal. Calcd. for $C_{21}H_{16}ON_2$: C, 80.73; H, 5.17. Found: C, 80.86; H, 5.25.

The diphenylhydrazone precipitated when 2.4 g. of the ketone, 4.3 g. of phenylhydrazine and 25 cc. of alcohol were heated for twelve hours; m. p. 157–160° after recrystallization from alcohol.

Anal. Calcd. for $C_{33}H_{28}ON_4$: C, 79.80; H, 5.69. Found: C, 79.83; H, 5.68.

Incidentally it was noticed that 2-(2'-hydroxybenzoyl)- and 2-(2'-methoxybenzoyl)-benzoic acids taste slightly bitter while the corresponding 4'-hydroxy¹³ and 4'-methoxy¹³ compounds are sweet. Methyl 2-(2'-methoxybenzoyl)- and methyl 2-(4'-methoxybenzoyl)-benzoate are tasteless.

Summary

It has been found that the acid chloride of 2-benzoylbenzoic acid reacts readily, at ordinary temperature, with a variety of phenols and aryl methyl ethers to yield diarylphthalides; in a few instances it was necessary to add aluminum chloride to the reaction mixture.

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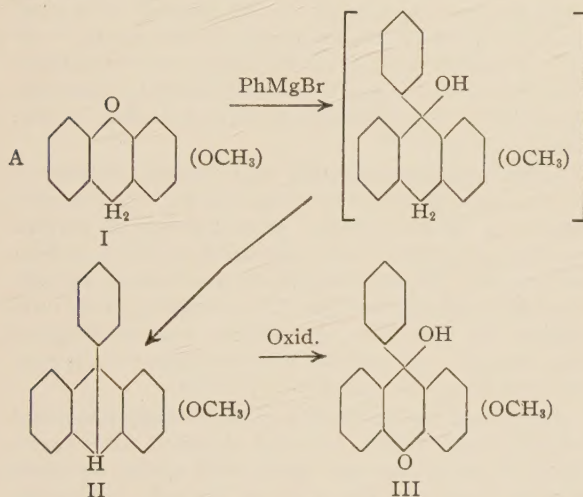
(13) Cohn, "Die organischen Geschmacksstoffe," Franz Siemenroth, Berlin, 1914, pp. 325, 327.

[CONTRIBUTION FROM THE COLLEGE OF PHARMACY, UNIVERSITY OF MICHIGAN]

Derivatives of 9-Hydroxy-9-phenylanthrone-10¹BY F. F. BLICKE AND R. D. SWISHER²

This investigation, the object of which was explained previously,³ represents a continuation of our study of anthrones.

By the use of reaction scheme A—interaction of 2-, 3- and 4-methoxyanthrone-9,⁴ (I), respectively, with phenylmagnesium bromide—the three anthracenes, 2-, 3- and 4-methoxy-9-phenylanthracene (II) and the 2-, 3- and 4-methoxy-9-hydroxy-9-phenylanthrone-10 (III) were prepared.



It was found by Jones and Root⁵ that diphenylphthalin and thionyl chloride yield 9-phenyl-9-chloroanthrone-10. Repetition of the experiment by us yielded similar results. In the event that 4',4''-dimethoxydiphenylphthalin and thionyl chloride behaved in the same manner 3-methoxy-9-chloro-9-(4'-methoxyphenyl)-anthrone-10 should be formed; hydrolysis of the chloro derivative should yield the corresponding 9-hydroxyanthrone. It was found, however, that instead of the anthrone there was formed 2-(4''-methoxybenzoyl)-4'-methoxybenzophenone.⁶

(1) This paper represents the third part of a dissertation which has been submitted to the Graduate School by Mr. Swisher in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the University of Michigan.

(2) The Upjohn Company Fellow.

(3) Blicke and Weinkauff, *THIS JOURNAL*, **54**, 1460 (1932).

(4) 4-Methoxyanthrone-9 may also be called 1-methoxyanthrone-10.

(5) Jones and Root. *THIS JOURNAL*, **48**, 183 (1926). The initial reaction product, the acid chloride of triphenylmethane-2-carboxylic acid, was also isolated by them.

(6) Ref. 3, p. 1457.

From 4'-methoxydiphenylphthalin and thionyl chloride there was obtained 3-methoxy-9-hydroxy-9-phenylanthrone-10 and 9-hydroxy-9-(4'-methoxyphenyl)-anthrone-10.⁷

It has been shown previously⁸ that when 4',4''-dimethoxy- or 4',4''-dihydroxydiphenylphthalin is treated with sulfuric acid and the reaction product obtained subjected to oxidation there are produced, respectively, 2-(4''-methoxybenzoyl)-4'-methoxy- and 2-(4''-hydroxybenzoyl)-4'-hydroxybenzophenone. We have discovered that 4'-methoxydiphenylphthalin, when treated with sulfuric acid, is converted into a yellow, amorphous product which yields intense blue-green fluorescent solutions. This material is undoubtedly 2-phenyl-5-(4'-methoxyphenyl)-benzofuran; upon oxidation the latter product was converted into 2-(4''-methoxybenzoyl)-benzophenone. In addition there was obtained from this reaction 9-hydroxy-9-(4'-methoxyphenyl)-anthrone-10.

Experimental Part

Methoxyanthrones.—2-Methoxyanthrone-9 was synthesized by ring closure of 2-(4'-methoxybenzyl)-benzoic acid.⁹ Upon oxidation¹⁰ of the anthrone, 2-methoxyanthraquinone was obtained; the latter, when treated with copper and sulfuric acid, yielded 3-methoxyanthrone-9.¹¹

In order to obtain 4-methoxyanthrone-9, 900 cc. of sulfuric acid diluted with 300 cc. of water was added to 90 g. of 2-(2'-methoxybenzyl)-benzoic acid.¹² The mixture was heated at 50° for one hour, poured into 8000 cc. of water, the precipitate filtered, washed with sodium bicarbonate solution, then with water and dried; yield 40 g.; m. p. 134–135° after recrystallization from alcohol. *Anal.* Calcd. for C₁₅H₁₂O₂: C, 80.32; H, 5.40. Found: C, 80.22; H, 5.43. Upon acidification of the bicarbonate solution 18 g. of unchanged acid was recovered.

1-Methoxyanthraquinone, which was required for another investigation, is obtained readily from 4-methoxyanthrone-9 as shown by the following experiment. To 40 g. of the crude anthrone, dissolved in 300 cc. of acetic

(7) Ref. 3, p. 1461.

(8) Ref. 3, p. 1456.

(9) Barnett, Goodway and Savage, *Ber.*, **64**, 2191 (1931); Ref. 3, p. 1462.

(10) Ref. 3, p. 1463.

(11) Attree and Perkin, *J. Chem. Soc.*, 152 (1931).

(12) This substance was obtained by reduction of 2-(2'-methoxybenzoyl)-benzoic acid with zinc and ammonia water according to the method used by Steyermark and Gardner [*THIS JOURNAL*, **52**, 4891 (1930)] for the reduction of the corresponding hydroxybenzoylbenzoic acid.

acid, there was added 40 g. of sodium dichromate, dissolved in a small amount of water. The mixture was heated for thirty minutes on a steam-bath, cooled, the precipitate filtered, washed with water and recrystallized from acetic acid; the anthraquinone weighed 32 g. and melted at 165–167°. ¹³

2-, 3- and 4-Methoxy-9-phenylanthracene.—To a benzene solution of the required methoxyanthrone there was added three times the calculated amount of phenylmagnesium bromide. The green, fluorescent mixture was heated for one hour, decomposed with ice and hydrochloric acid and subjected to steam distillation.

The crude, oily 2-methoxy compound was treated with ether and the ether solution separated from a small amount of insoluble, crystalline material. Acetic acid was added to the ether solution and after some time 2-methoxy-9-phenylanthracene separated in crystalline form.

The 3-methoxy compound was obtained in crystalline form in the manner described above. The 4-methoxy compound became solid during the steam distillation.

2-, 3- and 4-Methoxy-9-hydroxy-9-phenylanthrone-10.—The preparative procedure is illustrated only in the case of the 3-methoxy compound.

A mixture of 1.5 g. of 3-methoxy-9-phenylanthracene, 1.0 g. of sodium dichromate and 8 cc. of acetic acid was heated for fifteen minutes on a steam-bath. The mixture was cooled, the crystals filtered and washed with water; yield 1.5 g.

2-, 3- and 4-Methoxy-9-methoxy-9-phenylanthrone-10.—Hydrogen chloride was passed into the required methoxy-9-hydroxy-9-phenylanthrone-10, suspended in absolute methyl alcohol. The material soon dissolved. Upon concentration of the solution the 9-methoxy derivative separated in crystalline form.

When the various methoxyphenylanthrones were heated with acetic and hydrobromic acids in attempts to de-

methyrate them, dark colored, resinous, alkali-insoluble substances were obtained.

Compounds 1, 4, 5 and 6 were recrystallized from acetic acid, compound 2 from ethyl alcohol, compounds 7, 8 and 9 from methyl alcohol and compound 3 from a mixture of alcohol and ethyl acetate. Compounds 1, 2 and 3 were colored red by contact with concd. sulfuric acid and yield solutions which possess a blue fluorescence when dissolved in organic solvents. Compounds 4–9 turn blue when moistened with sulfuric acid.

4',4''-Dimethoxydiphenylphthalin and Thionyl Chloride.—To 17.5 g. of the phthalin there was added 100 cc. of dry benzene and 10 g. of thionyl chloride. After twelve hours the deep red solution was steam distilled, the yellow, granular residue washed with water and digested for several hours with hot sodium carbonate solution to remove unchanged phthalin. The product, 17 g., dissolved in organic solvents to form green fluorescent solutions due, undoubtedly, to the presence of a small amount of 2,5-di-(*p*-methoxyphenyl)-3,4-benzofuran. ¹⁴ After recrystallization from alcohol and several recrystallizations from acetic acid 2-(4''-methoxybenzoyl)-4'-methoxybenzophenone was obtained in the form of colorless needles; mixed m. p. 154–157°.

4'-Methoxydiphenylphthalin and Thionyl Chloride.—To 3 g. of the phthalin ¹⁵ there was added 75 cc. of benzene and 2 g. of thionyl chloride. After four days the benzene was removed and the residue digested with sodium carbonate solution. The undissolved material became partially crystalline after several days. The crystalline product was washed free from gum with acetone and recrystallized from alcohol. The product was 3-methoxy-9-hydroxy-9-phenylanthrone-10; mixed m. p. 176–178°.

In a second experiment 20 g. of the phthalin was mixed with an equal weight of thionyl chloride. After twelve hours the pasty mass was heated with sodium carbonate solution for several hours and the insoluble portion dissolved in acetone. After several days 4 g. of crystalline 9-hydroxy-9-(4'-methoxyphenyl)-anthrone-10 had separated; mixed m. p. 206–207°. ¹⁶

Treatment of 4'-Methoxydiphenylphthalin with Sulfuric Acid and Subsequent Oxidation of the Product Formed.—A mixture of 20 g. of the phthalin and 25 cc. of concd. sulfuric acid was stirred for five minutes, poured into 800 cc. of water, with vigorous agitation of the mixture, the yellow, amorphous product dissolved in 150 cc. of acetic acid and heated for a few minutes with 10 g. of sodium dichromate, dissolved in 10 cc. of water. The crystalline oxidation product, which separated, weighed 7.5 g. Upon recrystallization from acetic acid 2-(4''-methoxybenzoyl)-benzophenone was obtained; mixed m. p. 132–134°. ¹⁷ Careful dilution of the acetic acid filtrate yielded 3.5 g. of crystalline 9-hydroxy-9-(4'-methoxyphenyl)-anthrone-10 which was recrystallized three times from acetic acid; mixed m. p. 205–206°. ¹⁸

TABLE I

2-, 3- AND 4-METHOXY-9-PHENYLANTHRACENE (C ₂₁ H ₁₆ O)						
	M. p., °C.	Carbon, %		Hydrogen, %		
		Calcd.	Found	Calcd.	Found	
1 2-Methoxy	94–96 ^a	88.70	88.30	5.68	5.60	
2 3-Methoxy	106–108 ^b	88.70	88.52	5.68	5.68	
3 4-Methoxy	164–166	88.70	88.58	5.68	5.76	
2-, 3- AND 4-METHOXY-9-HYDROXY-9-PHENYLANTHRONE-10 (C ₂₁ H ₁₆ O ₃)						
4 2-Methoxy	183–185	79.71	79.51	5.10	5.18	
5 3-Methoxy	177–178	79.71	79.64	5.10	5.04	
6 4-Methoxy	228–230	79.71	79.72	5.10	5.14	
2-, 3- AND 4-METHOXY-9-METHOXY-9-PHENYLANTHRONE-10 (C ₂₂ H ₁₈ O ₃)						
7 2-Methoxy	115–117	79.96	79.63	5.50	5.53	
8 3-Methoxy	142–144	79.96	79.96	5.50	5.36	
9 4-Methoxy	194–195	79.96	79.98	5.50	5.51	

^a Since 2-methoxyanthrone-9 melts at 96–98° a portion of the latter was mixed with the anthracene; mixed m. p. 70–80°.

^b 3-Methoxyanthrone-9 melts at 105–106°; a mixture of the anthrone and the anthracene melted at 80–90°.

(13) Graebe and Bernhard [*Ann.*, **349**, 225 (1906)] reported 169.5°.

(14) Ref. 3, p. 1458.

(15) Blicke and Swisher, *THIS JOURNAL*, **56**, 924 (1934).

(16) Blicke and Weinkauff [*ibid.*, **54**, 1462 (1932)] reported the melting point as 206–207°.

(17) Blicke and Swisher, *ibid.*, **56**, 925 (1934), reported 133–135°.

(18) The recorded m. p. is 206–207° [Blicke and Weinkauff, *ibid.*, **54**, 1461 (1932)].

Summary

The following new compounds have been prepared; 4-methoxyanthrone-9, 2-, 3- and 4-methoxy-9-phenylanthracene, 2-, 3- and 4-methoxy-9-hydroxy-9-phenylanthrone-10 and 2-, 3-

and 4-methoxy-9-methoxy-9-phenylanthrone-10.

The interaction of 4'-methoxy- and 4',4''-dimethoxydiphenylphthalin with thionyl chloride and the action of sulfuric acid on 4'-methoxydiphenylphthalin has been investigated.

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